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Research Article

Clinical Findings and Vitamin D Levels in Children with Acute Rheumatic Fever

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Objective: Acute rheumatic fever (ARF) is an autoimmune disease and the leading cause of acquired heart disease in children living in low- and middle-income countries. Vitamin D deficiency has been reported in various autoimmune diseases. In this study, our objective was to assess clinical, laboratory and echocardiographic findings of patients with ARF, and to evaluate patients for vitamin D deficiency.

Materials and Methods: In this retrospective study spanning 21 years, children diagnosed with ARF and followed up were evaluated. Among them, patients whose vitamin D levels were measured at the time of diagnosis were compared with a healthy control group.

Results: Of the 244 patients included in the study, 116 (47.5%) were female, and 128 (52.5%) were male. Patients' mean (SD) age was 10.1 (±3.0) years. Recovery or regression of valve insufficiency was observed in 95 (46.3%) out of 205 patients with carditis. The sensitivity of the Jones Criteria increased from 86.5% to 95.5% with the last update. Among the 34 patients in whom vitamin D levels were measured, 91.2% of them were found to have deficient or insufficient levels. The median (IQR) vitamin D level was 10.0 (8.7) ng/mL in the patient group and 16.2 (8.9) ng/mL in the control group, with a statistically significant difference (P = .002).

Conclusion: Regular secondary prophylaxis may contribute to the improvement of valvular findings. The last revision of the Jones Criteria has increased diagnostic sensitivity in ARF. Vitamin D deficiency may play a role in the pathogenesis of the disease.

Keywords: Autoimmunity, Child, Jones criteria, Rheumatic fever, Vitamin D

1. INTRODUCTION

Acute rheumatic fever (ARF) is an autoimmune disease caused by infection with group A streptococcus (GAS) – *Streptococcus pyogenes.*[1] Although it is most commonly observed in children aged 5-15 years, it has been reported that ARF attacks may occur between the ages of 2 and 65 years.[2] Approximately 20 million people worldwide are affected by rheumatic heart disease (RHD), with 500,000 new cases of acute rheumatic fever (ARF) occurring each year. Furthermore, there are 233,000 annual deaths attributed to ARF or RHD.[1–4] The incidence of ARF in Türkiye ranges between 25 and 100 per 100,000 population, similar to rates observed in Mediterranean and Middle Eastern countries.[5] Many factors contribute to the development of ARF, including genetic predisposition, the virulence of the streptococcus bacteria, socioeconomic status, and household overcrowding.[3] Due to the similarity between some streptococcal antigens and human proteins, it is believed that ARF develops as a result of the inflammatory response generated by both humoral and cell-mediated immune systems.[6–9]

The Jones Criteria are utilized for the diagnosis of ARF and were revised by the American Heart Association in 2015 (Table 1).[10] Due to the heterogeneous nature of ARF worldwide, this modification defines different criteria for low-risk and moderate-to-high-risk populations. Low risk is defined as having an ARF incidence of less than 2 per 100,000 school-aged children per year or an all-age prevalence of RHD of less than or equal to 1 per 1000 population. All other populations are considered moderate to high risk. For initial ARF diagnosis, two major or one major plus two minor manifestations are required. In cases of recurrent ARF, two major or one major plus two minor manifestations, or three minor manifestations are diagnostic.[10]

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Table 1.

Jones criteria (2015 revision)

Major Criteria	
Low risk population	**Moderate and high risk population**
Carditis (clinical and/or subclinical)	Carditis (clinical and/or subclinical)
Arthritis (polyarthritis only)	Arthritis (monoarthritis, polyarthritis or polyarthralgia)
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
Minor Criteria	
Low risk population	**Moderate and high risk population**
Polyarthralgia	Monoarthralgia
Fever (≥38.5°C)	Fever (≥38°C)
ESR ≥60 mm/h and/or CRP ≥3.0 mg/dL	ESR ≥30 mm/h and/or CRP ≥3.0 mg/dL
Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)

CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate

Vitamin D plays a crucial role in calcium homeostasis and maintaining bone mineral density.[11] However, researches has demonstrated that Vitamin D also possesses antiproliferative, proapoptotic, anti-inflammatory, and immunomodulatory functions.[12,13] It plays an important role in both the innate and acquired immune systems, and its deficiency has been associated with an increased tendency toward autoimmune diseases.[14]

The aim of our study was to assess the demographic, clinical, and laboratory findings of patients with ARF, and to evaluate patients for vitamin D deficiency.

2. MATERIAL AND METHODS

2.1. Study design

This study was conducted at the Department of Pediatric Cardiology, Marmara University, Istanbul, Türkiye. Patients who were followed up in our clinic with a diagnosis of ARF between May 1995 and June 2016 were evaluated retrospectively. Patients were assessed according to the Modified Jones Criteria. After 2015, new diagnostic criteria were implemented. However, in our clinics, echocardiography was routinely performed for all patients with ARF as part of the initial diagnostic work-up. Valvular regurgitations exceeding the physiologic criteria were considered evidence of carditis even before the 2015 update.

The results of patients whose vitamin D levels were measured at the time of diagnosis were compared with those of a healthy control group. The control group comprised children of the same age and gender who were randomly selected from those presenting to the general pediatric outpatient clinic at the same time, without chronic diseases or vitamin D replacement.

Patients' demographic and clinical data were extracted from their medical records. Laboratory tests included complete blood count, antistreptolysin O (ASO), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), 25(OH) vitamin D, calcium, phosphorus, alkaline phosphatase levels, throat culture, and rapid group A streptococcal carbohydrate antigen test results. Telecardiography, electrocardiography, and echocardiography findings were also documented. Laboratory tests were conducted using Beckman Coulter DxH800, AU680, Siemens BN II, and Hitachi Modular E170 equipment. Philips iE33 was used as the

echocardiography machine since 2010, and Philips Envisor C was used before.

2.2. Ethics of the study

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Marmara University Faculty of Medicine Clinical Research Ethics Committee, İstanbul, Türkiye (Date: 04 March 2016/No: 09.2016.180).

2.3. Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics 17.0 (IBM Corp.). Descriptive statistics were expressed as number (%), mean ± standard deviation (SD) and/or median with interquartile range (IQR) (depending on data distribution). Vitamin D levels were compared between the patient and control groups using the Mann-Whitney U test. A P-value of <.05 was considered statistically significant.

3. RESULTS

In the study, 244 patients were included, of whom 116 (47.5%) were female and 128 (52.5%) were male. The mean (SD) age of the patients was 10.1 (±3.0) years. The median (IQR) follow-up period was 2.4 (3.1) years, with 23 patients (9.4%) being out of regular follow-up. Regarding the season of ARF diagnosis, 42.2% occurred in winter, 25.4% in spring, 18.9% in summer, and 13.5% in autumn.

The most common symptom reported was joint complaints, observed in 204 (83.6%) patients. Among other symptoms, 92 (37.7%) patients experienced fever, 34 (13.9%) reported chest pain, 30 (12.2%) had palpitations, 27 (11%) exhibited involuntary movements, 27 (11%) complained of fatigue, 6 (2.4%) experienced abdominal pain, and 5 (2%) had a rash.

Carditis was the most common major manifestation, detected in 205 patients (84%). Other major manifestations included arthritis in 134 patients (54.9%), chorea in 27 patients (11%), erythema marginatum in 5 patients (2%), and subcutaneous nodules in 3 patients (1.2%). These results were similar across both genders. Prolonged PR interval was not utilized as a minor manifestation in patients with carditis. Among the 110 patients without arthritis, 66 (60%) reported polyarthralgia, while 4 (3.6%) reported monoarthralgia. In the presence of other major findings, while acute phase reactant (APR) levels tend to be elevated, among the 24 patients with chorea and APR results, only 8 (33.3%) had elevated APR levels. The major and minor manifestations are summarized in Table 2.

Table 2.

The major and minor manifestations of the study sample

Major manifestations		**Minor manifestations**	
	n (%)		*n* (%)
Carditis	205 (84)	Fever	92 (37.7)
Arthritis	134 (54.9)	Arthralgia	70 (28.7)
Chorea	27 (11)	Prolonged PR interval	41 (16.8)
Erythema marginatum	5 (2)	Increase in acute phase reactants	164 (67.2)
Subcutaneous nodules	3 (1.2)		

Among the 205 patients with carditis, 129 (62.9%) had involvement of a single valve, 69 (33.7%) had involvement of two valves, and 7 (3.4%) had involvement of three valves. Mitral regurgitation was present in 195 patients (95.1%), aortic regurgitation in 84 patients (41%), and tricuspid regurgitation in 9 patients (4.4%). 159 (77.6%) patients had mild carditis, 30 (14.6%) had moderate carditis, and 16 (7.8%) had severe carditis. There was no difference between genders in all three groups. 40 (19.5%) patients had silent carditis, and 6 (2.9%) had indolent carditis.

Recovery or regression of valve insufficiency was detected in 95 (46.3%) out of 205 patients with carditis (Table 3). During the follow-up of patients with mild carditis, 27 (17%) of them completely recovered from signs of valve insufficiency, and 43 (27%) experienced regression. Among those with moderate carditis, 5 (16.7%) experienced complete recovery from signs of valve

insufficiency, and 14 (46.7%) regressed. None of the patients with severe carditis experienced recovery from signs of valve insufficiency. Six patients (37.5%) showed regression, while 2 patients (12.5%) experienced progression of valve insufficiency, leading to valve replacement in these cases.

Table 3.

Changes in the signs of valve insufficiency according to carditis severity

Carditis severity	Changes in carditis				Unfollowed
	Recovery *n* (%)	Regression *n* (%)	Unchanged *n* (%)	Progression *n* (%)	*n* (%)
Mild (n=159)	27 (17.0)	43 (27.0)	73 (45.9)	1 (0.6)	15 (9.5)
Moderate (n=30)	5 (16.7)	14 (46.7)	9 (30.0)	0	2 (6.6)
Severe (n=16)	0	6 (37.5)	8 (50.0)	2 (12.5)	0
Total (n=205)	32 (15.6)	63 (30.8)	90 (43.9)	3 (1.5)	17 (8.2)

Monoarthritis was found in 39 (29.1%) out of 134 patients with arthritis. Sixty (44.8%) patients had involvement of two joints, 20 (14.9%) patients had involvement of three joints, and 15 (11.2%) patients had involvement of four or more joints. Among the 27 patients with chorea, 15 (55.6%) were between the ages of 11-15. Erythema marginatum was present in 5 (2%) of the patients, and subcutaneous nodules were present in 3 (1.2%) of them; however, these alone were not detected major manifestations.

Recurrence was detected in 16 (6.6%) patients during follow-up. Among these patients, 15 (93.7%) were irregularly using secondary prophylaxis. While 86.5% of the patients fully met the criteria according to the old Jones criteria, this rate increased to 95.5% with the 2015 update.

Laboratory results are presented in Table 4.

Table 4.

Laboratory results of the study sample

	n	Mean ± SD	Median (IQR)	Range
ASO (IU/mL)	239	781.6 ± 597.2	600.0 (650.0)	66 - 4060
Anti-DNase B (IU/mL)	18	879.1 ± 458.4	781.0 (592.0)	255 - 2100
ESR (mm/hour)	169	62.7 ± 34.5	60.0 (53.0)	2 - 145
CRP (mg/L)	146	58.6 ± 60.0	35.0 (77.3)	0.1 - 346
WBC (/mm^3)	171	10272.6 ± 3318.5	9600.0 (4100.0)	4000 - 22100
Hemoglobin (g/dL)	171	11.6 ± 1.2	11.6 (2.0)	9.1 - 14.6
Platelet (/mm^3)	171	349.0 ± 106.4	336.0 (150.0)	141 - 618

Anti-DNase B = Anti-deoxyribonuclease B; ASO = Antistreptolysin O; CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate; IQR = Interquartile range; SD = Standard deviation; WBC = White blood cell

In the group of 34 patients in whom vitamin D levels were measured, 15 (44.1%) were female. The mean (SD) age was 11.2 (±2.9) years in the patient group and 11.1 (±2.8) in the control group. The median (IQR) of vitamin D level was 10.0 (8.7) ng/mL in the patient group and 16.2 (8.9) ng/mL in the control group, with a statistically significant difference (P = .002). The mean (SD) calcium, phosphorus, and alkaline phosphatase levels of the patients were 9.4 (±0.37) mg/dL, 4.3 (±0.73) mg/dL, and 154.3 (±54.3) U/L, respectively, and were within normal limits. Of the patients, 30 (88.2%) had carditis, while in 4 (11.8%) patients, arthritis alone was the major manifestation. 18 (53%) patients had both carditis and arthritis, and 2 (5.9%) had carditis and chorea simultaneously.

31 (91.2%) of ARF patients had deficient or insufficient levels of vitamin D (Table 5). Furthermore, all severe carditis cases had vitamin D levels below 15 ng/mL.

Table 5.

The comparison of vitamin D levels

25(OH)Vitamin D	**Patients** *n* (%)	**Controls** *n* (%)
Severe deficient (<5 ng/mL)	7 (20.6)	0
Deficient (5-15 ng/mL)	17 (50.0)	16 (47.1)
Insufficient (15-20 ng/mL)	7 (20.6)	11 (32.3)
Normal (20-80 ng/mL)	3 (8.8)	7 (20.6)
Total	34 (100)	34 (100)

4. DISCUSSION

In the present study, which included 21 years of patient data from a tertiary pediatric cardiology center, we comprehensively evaluated the clinical, laboratory, and echocardiographic findings of children with ARF. One of the most important findings was the improvement in carditis in nearly half of the patients, highlighting the effectiveness of early initiation of secondary prophylaxis in preventing disease progression. Additionally, the observation of lower vitamin D levels in patients compared with the control group suggests a possible role of vitamin D deficiency in the pathogenesis of the disease.

Our analysis revealed that recovery or regression of valvular insufficiency was observed in 46.3% of patients with carditis during a median follow-up of 2.4 (IQR 3.1) years. Meira et al.[15] reported regression in 59.4% of patients with mild valve lesions and in 15.7% of those with moderate lesions over a follow-up period of 2–15 years. In addition, a recent review (2024) further supported the efficacy of secondary prophylaxis.[16] Unlike the findings of Meira et al.[15], our study demonstrated improvement not only in mild but also in moderate valvular lesions, underscoring the importance of secondary prophylaxis in altering disease progression.

We observed a recurrence rate of 6.5%, with the vast majority (93.5%) of recurrent cases occurring in patients who had discontinued regular prophylaxis. Recurrence rates have been reported to vary between 8.5% and 40% in different studies.[5,17–19] In the study by Pirinccioglu et al.[18], recurrences were observed in 78% of patients with ARF who did not receive regular secondary prophylaxis, while the overall recurrence rate among all ARF patients was 34.9%. Beyond its role in improving valvular lesions, secondary prophylaxis also prevents ARF recurrence and stands out as the most critical and unique factor influencing disease course, with its efficacy firmly established in the literature.[20,21]

Most of our patients were diagnosed in winter (42.2%), followed by spring (25.4%). Given that ARF typically develops after a latent period of 1–5 weeks following tonsillitis or pharyngitis caused by GAS, the disease is expected to occur more frequently in winter and spring, when streptococcal infections are most common.[2] Consistent with the literature, our findings also demonstrated that diagnoses were most frequent during these two seasons.

In our cohort, joint complaints were the most common presenting symptom (83.6%). In contrast, Seckeler et al.[19] reported fever as the most frequent symptom (80.8%). Several studies conducted in Türkiye have similarly identified joint complaints as the predominant manifestation.[17,22] Our findings are therefore consistent with national data, emphasizing that ARF should always be considered in patients presenting with joint complaints.

Carditis was the most common major manifestation in our study (84%). In the literature, reported frequencies of major manifestations vary, with carditis observed in 55–82.2% of cases, arthritis in 55–72%, chorea in 4.4–28%, erythema marginatum in 0.5–2%, and subcutaneous nodules in 0.5–6.2%.[5,17,22–24] The higher rate of carditis in our study may be explained by the routine use of echocardiography for all patients with suspected ARF in our clinic.

In our study, mitral regurgitation was present in 95.1% of cases, and aortic regurgitation was

observed in 41% of patients. In the literature, the mitral valve is most frequently involved, followed by the aortic valve. Although regurgitation is observed during the acute phase of the illness, stenosis may develop later due to fibrosis, particularly in individuals over 30 years of age.[25] Consistent with the literature, in our pediatric cohort, the mitral valve was most commonly affected, followed by the aortic valve, and all patients with carditis exhibited valvular regurgitation. None of the patients had valve stenosis.

Based on our data, the rate of silent carditis was 19.5%. In studies conducted in Türkiye, the prevalence of silent carditis has been reported to range from 22.4% to 31.3%.[26–28] The proportion of silent carditis in our study is similar to the findings reported by Tubridy-Clark et al.[29], which involved a larger patient population. If these patients do not receive appropriate prophylactic treatment, valve involvement may progress.[29,30] In addition to detecting silent carditis, echocardiographic imaging also helps distinguish innocent murmurs and congenital heart diseases, which can lead to false diagnoses of carditis. Echocardiography is crucial for understanding valve lesions during the diagnosis and follow-up of ARF. Therefore, silent carditis has been recognized as a major manifestation in all populations according to the Jones criteria updated in 2015.[10]

In our study, while 86.5% of the patients fully met the criteria according to the old criteria, this rate increased to 95.5% with the 2015 update. Jones criteria are employed in the diagnosis of ARF. If the criteria from 1992 were strictly adhered to, it is estimated that 78-87% of patients could be diagnosed.[31,32] In a study by Seckeler et al.[19], 75% of ARF patients fully met these criteria. For these reasons, the New Zealand Criteria were developed in 2008, and the Australian Criteria were developed in 2006 and updated in 2012.[31,33] Finally, the Jones Criteria were updated by the American Heart Association in 2015.[10] This update, which stratifies populations into low- and moderate-to-high-risk groups, facilitates easier diagnosis based on the region in which the patient resides.

According to our results, vitamin D levels were insufficient or deficient (<20 ng/ml) in 91.2% of patients with ARF, significantly lower than those in the control group. Vitamin D has been demonstrated to possess antiproliferative, proapoptotic, anti-inflammatory, and immunomodulatory functions in recent research.[12,13] Vitamin D deficiency has been linked to various autoimmune diseases, including Type 1 diabetes, multiple sclerosis, Crohn's disease, systemic lupus erythematosus, and rheumatoid arthritis. Research suggests that these diseases are more prevalent in individuals with vitamin D deficiency.[34–37] Low vitamin D levels were also found in patients with ARF and RHD.[38–40] ARF is an autoimmune disease, and the observation of low vitamin D levels in children with ARF in our study supports the findings of other studies reported in the literature.

Although Türkiye is located in a geographical area where sunlight is abundant, factors such as urbanization, reduced outdoor activities, and the use of UV-blocking creams and clothing covering most of the body can diminish the benefits of sunlight exposure and lead to vitamin D deficiency. The American Academy of Pediatrics recommends a daily intake of 400 IU of vitamin D for ages 0-1 and 600 IU for ages 1-18.[41] Recognizing and treating deficiencies in children could be beneficial in preventing ARF and other autoimmune diseases.

The retrospective nature of our study constitutes a limitation. Although the control group was selected from a healthy population without chronic diseases, BMI and nutritional status were not assessed in patients and controls, which is a limitation of this study. Vitamin D levels between patients with and without carditis could not be statistically evaluated in our study due to the small number of patients in these groups.

5. CONCLUSION

Consistent secondary prophylaxis may contribute to improvements in valvular findings. The last update of the Jones Criteria has enhanced the diagnostic sensitivity in ARF. Further prospective studies are warranted to elucidate the potential role of vitamin D deficiency in the pathogenesis of

ARF, and to determine whether it exacerbates clinical manifestations.

Article Information Form

Authors' Contribution

Conceptualization, Methodology: EÇ, NÇÇ, FA; Writing original draft: EÇ, FA; Review and editing; EÇ, NÇÇ, FA; Visualization: EÇ, FA; Supervision: EÇ, FA; Investigation and data curation: EÇ, NÇÇ, FA; Formal analysis: EÇ, NÇÇ, FA, Resources; EÇ, FA; Validation: EÇ, NÇÇ, FA; Project administration: EÇ, FA.

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Ethics Committee Approval

Ethical approval was obtained from the Clinical Research Ethics Committee of Marmara University Faculty of Medicine (Approval No: 09.2016.180)

Artificial Intelligence Statement

No artificial intelligence tools were used while writing this article.

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REFERENCES

1. Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. *Lancet*. 2005;366(9480):155-68. doi:10.1016/S0140-6736(05)66874-2
2. Akalin F. Akut Romatizmal Ateş ve Yenilikler. *Turk Pediatri Ars*. 2007;42:85-93.
3. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis.* 2005;5(11):685-94. doi:10.1016/S1473-3099(05)70267-X
4. Tibazarwa KB, Volmink JA, Mayosi BM. Incidence of acute rheumatic fever in the world: A systematic review of population-based studies. *Heart*. 2008;94(12):1534-40. doi:10.1136/hrt.2007.141309
5. Ozer S, Hallioğlu O, Ozkutlu S, Celiker A, Alehan D, Karagöz T. Childhood acute rheumatic fever in Ankara, Turkey. *Turk J Pediatr.* 2005;47(2):120-4.
6. Cunningham MW. Pathogenesis of group A streptococcal infections. *Clin Microbiol Rev.* 2000;13(3):470-511. doi:10.1128/CMR.13.3.470
7. Cunningham MW. Autoimmunity and molecular mimicry in the pathogenesis of post-streptococcal heart disease. *Front Biosci.* 2003;8:s533-43. doi:10.2741/1067
8. Guilherme L, Oshiro SE, Fae KC, et al. T-cell reactivity against streptococcal antigens in the periphery mirrors reactivity of heart-infiltrating T lymphocytes in rheumatic heart disease patients. *Infect Immun*. 2001;69(9):5345-51. doi:10.1128/iai.69.9.5345-5351.2001
9. Fae KC, Oshiro SE, Toubert A, Charron D, Kalil J, Guilherme L. How an autoimmune reaction triggered by molecular mimicry between streptococcal M protein and cardiac tissue proteins leads to heart lesions in rheumatic heart disease. *J Autoimmun.* 2005;24(2):101-9. doi:10.1016/j.jaut.2005.01.007
10. Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: A scientific statement from the American Heart Association. *Circulation.* 2015;131:1806-18. doi:10.1161/CIR.0000000000000205
11. Winzenberg TM, Powell S, Shaw KA, Jones G. Vitamin D supplementation for improving bone mineral density in children. Cochrane Database Syst Rev. 2010;(10):CD006944. doi:10.1002/14651858.CD006944.pub2
12. Vojinovic J, Cimaz R. Vitamin D—update for the pediatric rheumatologists. *Pediatr Rheumatol Online J.* 2015;13:18. doi:10.1186/s12969-015-0017-9
13. Ozkan B, Doneray H. D vitamininin iskelet sistemi dışı etkileri. *Çocuk Sağlığı ve Hastalıkları Dergisi.* 2011;54:99-119.
14. Bikle DD. Vitamin D: Newly discovered actions require reconsideration of physiologic requirements. *Trends Endocrinol Metab.* 2010(6):375-84. doi:10.1016/j.tem.2010.01.003
15. Meira ZM, Goulart EM, Mota Cde C. Comparative study of clinical and doppler echocardiographic evaluations of the

progression of valve diseases in children and adolescents with rheumatic fever. *Arq Bras Cardiol*. 2006;86:32-8. doi:10.1590/s0066-782x2006000100006

16. Francia CJ, Fraser JF, Justo R, Cassimatis J, Manoy S, Johnston LM. Follow-up echocardiographic changes in children and youth aged <25 years with latent rheumatic heart disease: A systematic review and meta-analysis of global data. *Int J Cardiol*. 2024;403. doi:10.1016/j.ijcard.2024.131911
17. Gungor S, Doksoz O, Fettah A, Nacaroğlu HT, Orun UA, Karademir S. Akut romatizmal ateş tanısı ile izlenen hastaların geriye dönük olarak değerlendirilmesi: Beş yıllık tek merkez deneyimi. *İzmir Dr. Behçet Uz Çocuk Hast. Dergisi.* 2014;4:87-96.
18. Gözü Pirinççioğlu A, Alyan O, Kanğın M, et al. A retrospective investigation of clinical and laboratory findings in children with acute rheumatic fever, reactivation and compliance with prophylaxis. *Archives of the Turkish Society of Cardiology (Turk Kardiyol Dern Ars).* 2012;40(5):427-35. doi:10.5505/tkda.2012.87405
19. Seckeler MD, Barton LL, Brownstein R. The persistent challenge of rheumatic fever in the Northern Mariana Islands. *Int J Infect Dis.* 2010;14(3):e226-9. doi:10.1016/j.ijid.2009.04.003
20. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: A scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: Endorsed by the American Academy of Pediatrics. *Circulation*. 2009;119(11):1541-51. doi:10.1161/CIRCULATIONAHA.109.191959
21. Steer AC, Colquhoun S, Kado J, Carapetis JR. Secondary prophylaxis is important for the prevention of recurrent rheumatic fever in the Pacific. *Pediatr Cardiol.* 2011;32(6):864-5. doi:10.1007/s00246-011-9966-z
22. Orun UA, Ceylan O, Bilici M, et al. Acute rheumatic fever in the Central Anatolia Region of Turkey: A 30-year experience in a single center. *Eur J Pediatr.* 2012;171(2):361-8. doi:10.1007/s00431-011-1555-x
23. Carapetis JR, Currie BJ. Rheumatic fever in a high incidence population: The importance of monoarthritis and low grade fever. *Arch Dis Child.* 2001;85(3):223-7. doi:10.1136/adc.85.3.223
24. Chockalingam A, Gnanavelu G, Elangovan S, Chockalingam V. Current profile of acute rheumatic fever and valvulitis in southern India. *J Heart Valve Dis.* 2003;12:573-6.
25. Zühlke L, Engel ME, Karthikeyan G, Rangarajan S, Mackie P, Cupido B, et al. Characteristics, complications, and gaps in evidence-based interventions in rheumatic heart disease: The Global Rheumatic Heart Disease Registry (the REMEDY study*). Eur Heart J.* 2015;36(18):1115-22a. doi:10.1093/eurheartj/ehu449
26. Olgunturk R, Canter B, Tunaoglu FS, Kula S. Review of 609 patients with rheumatic fever in terms of revised and updated Jones criteria. *Int J Cardiol.* 2006;112(1):91-8. doi:10.1016/j.ijcard.2005.11.007
27. Pekpak E, Atalay S, Karadeniz C, Demir F, Tutar E, Uçar T. Rheumatic silent carditis: Echocardiographic diagnosis and prognosis of long-term follow up. *Pediatr Int.* 2013;55(6):685-9. doi:10.1111/ped.12163
28. Ozdemir O, Isik S, Abaci A, et al. Akut romatizmal ateşte sessiz düşman: Subklinik kardit. Arch Turk Soc Cardiol 2011; 39; 41-6.
29. Tubridy-Clark M, Carapetis JR. Subclinical carditis in rheumatic fever: A systematic review. *Int J Cardiol.* 2007;119(1):54-8. doi:10.1016/j.ijcard.2006.07.046
30. Ozkutlu S, Hallioglu O, Ayabakan C. Evaluation of subclinical valvar disease in patients with rheumatic fever. *Cardiol Young.* 2003;13:495-9.
31. Atatoa-Carr P, Lennon D, Wilson N; New Zealand Rheumatic Fever Guidelines Writing Group. Rheumatic fever diagnosis, management, and secondary prevention: A New Zealand guideline. *N Z Med J.*

2008;121(1271):59-69.
32. Pereira BA, da Silva NA, Andrade LE, Lima FS, Gurian FC, de Almeida Netto JC. Jones criteria and underdiagnosis of rheumatic fever. *Indian J Pediatr.* 2007;74(2):117-21. doi:10.1007/s12098-007-0001-6
33. RHDAustralia (ARF/RHD writing group), National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd ed). 2012.
34. Hyppönen E, Läärä E, Reunanen A, Järvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: A birth-cohort study. *Lancet*. 2001;358:1500-3. doi:10.1016/S0140-6736(01)06580-1
35. Munger KL, Levin LI, Hollis BW, Howard NS, Ascherio A. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. *JAMA*. 2006;296(23):2832-8. doi:10.1001/jama.296.23.2832
36. Iruretagoyena M, Hirigoyen D, Naves R, Burgos PI. Immune response modulation by Vitamin D: Role in systemic lupus erythematosus. *Front Immunol.* 2015;6:513. doi:10.3389/fimmu.2015.00513
37. Wöbke TK, Sorg BL, Steinhilber D. Vitamin D in inflammatory diseases. *Front Physiol.* 2014;5:244. doi:10.3389/fphys.2014.00244
38. Onan SH, Demirbilek H, Aldudak B, Bilici M, Demir F, Yılmazer MM. Evaluation of vitamin D levels in patients with acute rheumatic fever. *Anatol J Cardiol.* 2017(1):75-76. doi:10.14744/AnatolJCardiol.2017.7720
39. Thorup L, Hamann SA, Tripathee A, et al. Evaluating Vitamin D levels in Rheumatic Heart Disease patients and matched controls: A case-control study from Nepal. *PLoS One*. 2020;15(8):e0237924. doi:10.1371/journal.pone.0237924
40. Yusuf J, P J, Mukhopadhyay S, Vignesh V, Tyagi S. Evaluation of serum 25-hydroxyvitamin D levels in calcific rheumatic mitral stenosis- A cross sectional study. *Indian Heart J.* 2018;70(2):206-213. doi:10.1016/j.ihj.2017.06.010
41. American Academy of Pediatrics. Statement of endorsement. Dietary reference intakes for calcium and vitamin D. *Pediatrics*. 2012; 130: e1424. doi:10.1542/peds.2012-2590